Subject: Second Generation Antihistamine Open Hearing Statement
Response to Open Hearing Request for Comments:
May 11, 2001 FDA Advisory Committee Meeting
OTC Switch for Second Generation Antihistamines

To the Committee:

My name is Dr. Joel Hay. I am Associate Professor in the Department of Pharmaceutical Economics and Policy in the University of Southern California School of Pharmacy with a joint appointment in the USC Department of Economics. I have PhD, MPhil and MA degrees from the Yale University Department of Economics, and a BA in Economics from Amherst College.

I have worked in the health economics and pharmaceutical economics field for the past 25 years. I am a founding member and Executive Board Member of the non-profit organization, the International Society for Pharmacoeconomics and Outcomes Research, and Editor-in-Chief of its journal, Value in Health.

The views that I express are my own, and are not necessarily endorsed by any organization or enterprise with which I am affiliated.

Disclosures:

I have never been an investigator for any first or second generation antihistamine. I do not own stock in any company that sells or distributes antihistamines except possibly through retirement equity mutual funds. My presentation was covered, in part, by Aventis Pharmaceuticals.

I have consulted in the past with Wellpoint Health Networks, and have served on their Pharmaceutical Economics Advisory Board. My wife works for Wellpoint Health Networks. I am a Wellpoint consumer as well. I am a current enrollee in the Blue Cross of California Health Care and Pharmacy Benefit Plan. Blue Cross of California is a wholly-owned subsidiary of Wellpoint Health Networks.

Our academic department at USC receives research contract and grant funding, and graduate student fellowship support from many major pharmaceutical companies and managed care organizations, including Aventis and Wellpoint.

Comments on Rx-to-OTC Switch:

The FDA Hearing Request Letter states:
... the FDA is NOT seeking advice on economic considerations of a switch... Rather, the FDA is seeking advice from the committees on whether these agents ... could be used appropriately and safely by consumers without the intervention of a learned intermediary. In my view, public health and safety issues often cannot be neatly severed from economic considerations. In considering a non-sedating antihistamine (NSA) OTC switch, there are unique economic and market circumstances for this therapeutic class that may exacerbate public safety concerns. As I will discuss, the existing body of literature suggests that such a switch may lead to greater health risks for many Americans. The evidence implies that those at greatest increased risk are the poor, the frail elderly, the uneducated, and those with comorbidities, particularly asthma and sinusitis.

First, a unique aspect of this Citizen Petition to force an OTC switch needs to be underscored. Only once before in the past twenty years has the FDA agreed to switch a patented product (metaproterenol) from prescription to OTC status, and that was done with the cooperation of the product manufacturer. The public generally expects drug prices to fall substantially when an Rx-to-OTC switch occurs. This has certainly been the case in the past decade with the popular switches for the H2 receptor antagonists (e.g., ranitidine, cimetidine, famotidine), and with NSAIDS such as naproxen and ibuprofen.

However, for all of these prior Rx-to-OTC switches, patent protection for the brand name product was expiring at the time of the OTC product launch. The patent-holder was facing real or threatened competition from generic manufacturers, and decided to overcome this competition by increasing revenue in the OTC marketplace. In this current situation, all of the NSA products under consideration (loratadine, fexofenadine, and certirizine) still maintain market patent protection. There is no guarantee that switching them to OTC status will cause much, if any, reduction in wholesale acquisition price, since there will be no generic competition threat to force them to lower prices or to market a cheaper generic substitute. An Rx-to-OTC switch will not impact whatever competition exists between the three manufacturers currently.

Dr. Seidman was reported as having estimated that the NSA Rx-to-OTC switch will save Wellpoint Health Networks $80 million annually.[1] After an Rx-to-OTC switch, Dr. Seidman would tell California Blue Cross subscribers, such as myself, suffering allergic rhinitis that Blue Cross does not cover OTC medications. We would have to pay the $1.92 to $2.49 per day,[2] (potentially $75 per month) out of our own pockets should we need these NSA medications, rather than the current $15 co-pay for covered brand-name prescriptions.

For those of us who are well-off and well-informed, this will not be a significant reason to avoid these products. However, for the low-income and less-educated, including those currently covered by Medicaid or by Medicare managed care plans, VA, Indian Health Service and many other third party payers, there will likely be a substantial switching from covered prescription non-sedating antihistamines to non-covered OTC sedating antihistamines. The current NSA prices are 3 to ten times higher than the price for sedating antihistamines, such as diphenhydramine HCl (25 mg), which can be purchased for as little as $0.07 per tablet.[3]

It is well established that prescription drug consumption is highly sensitive to price and insurance coverage.[4-7] Based on a study of Medicare recipients, Stuart and Grana report that low-income elderly without supplemental drug insurance coverage are 40% less likely to use prescription medications than higher income (>$18,000 annual income) elderly with supplemental drug coverage.[8] They also found that the odds ratio for use of prescription medications to treat cold and allergies was (1.83: 95% CI 1.24-2.69) among elderly with drug insurance coverage compared to those without.

By eliminating drug benefit insurance coverage, the NSA Rx to OTC switch will increase price and reduce demand for loratadine, fexofenadine, and certirizine. This, in turn, will increase demand for the cheaper sedating OTC medications, such as diphenhydramine, particularly among those with low income and/or high out-of-pocket medical expenses. Increased use of sedating antihistamines will impose greater public health and safety risks, and a reduction in workforce productivity.[9-11]

In fact, Weiler et al. demonstrate in a driving simulator study that operating a motor vehicle while taking fexofenadine was statistically equivalent to operating a motor vehicle on placebo. However, study participants taking diphenhydramine performed significantly more poorly than those with blood alcohol levels of

0.1% (higher than the legal blood alcohol limit in all states). Moreover, diphenhydramine users had poorer driving simulator performance whether or not they exhibited drowsiness and sedation symptoms.

Allergic rhinitis afflicts more than 39 million persons in the US annually.[12] The US age-adjusted injury death rate is 49.1 per 100,000 population.[13] If even 10 percent of this patient population switches from NSAs to sedating antihistamines as a result of the Rx-to-OTC switch, the number of additional injury-related deaths in the US could increase by hundreds per year. This would be in addition to the increase in non-fatal injuries, lost work productivity, and property damage.

Upper income consumers may prefer the convenience of avoiding a doctor visit and getting their NSA medication without prescription at their pharmacy or supermarket. Doctor visit travel and waiting time are often more important factors to them than out-of-pocket medication costs. But for the poor, the frail elderly, and those with high medical utilization, out-of-pocket medication costs can make the difference between having and not having enough money to pay basic monthly bills. It is precisely these most vulnerable consumers who will be at increased risk of accident and injury to themselves and others due to increased use of sedating antihistamines.

Impact on Allergic Rhinitis Patients with Comorbidities

Moving NSAs from prescription status to OTC means that doctors and other learned intermediaries will no longer interact with patients choosing this therapeutic option. There are certain groups of AR patients, particularly those with comorbidities such as asthma and sinusitis, who may misdiagnose their condition, or experience additional disease complications if they are no longer regularly monitored by a physician for their AR treatment. Such patients may use newly available NSA OTC treatments to delay or postpone essential therapy for their asthma or sinusitis, leading to acute or chronic exacerbation of their medical conditions.

A recent study by Paramore et al. found that patients under medical treatment for comorbid AR and asthma actually had significantly lower hospitalization costs than matched patients with asthma alone.[14] The implication of this result is that routine physician management of both conditions together may actually be more cost effective (and is associated with fewer hospitalizations) than management of asthma alone. The increased contact between comorbid AR-asthma patients and health care

professionals appears to lead to better outcomes than would be expected if these patients were self-medicating their AR symptoms.

While these data are not conclusive in showing causation, they raise a caution about the safety of an Rx-to-OTC switch for these comorbid AR patients. More study is needed on the effect of increased self-medication by AR patients with comorbidities such as asthma and sinusitis to ensure that these patients are not at increased hospitalization risk when self-medicating their AR symptoms. Since 77% of the annual US hospitalization days associated with AR are due to comorbid asthma, this is a significant potential safety concern.[15] Rigorous studies evaluating the safety effects of reduction in physician management should be developed before the FDA makes a decision that might well result in increased hospitalization risk for comorbid AR patients.

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